Patent Assignment Abstract of Title

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Inventors: Aruna K. Behera, Hiroto Matsuse, Mukesh Kumar, Shyam S. Mohapatra

Title: Interrupting the interaction of intercellular adhesion molecule-1 and respiratory syncytial virus for prevention and treatment of infection

Assignment: 1

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MATSUSE, HIROTO **Exec Dt:** 10/02/2000

KUMAR, MUKESH **Exec Dt:** 09/01/2000

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Search Results as of: 5/12/2003 9:37:01 A.M.

5 ANSWER 1 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AB The respiratory syncytial virus (**RSV**) causes potentially fatal lower respiratory tract infection in infants. The molecular mechanism of **RSV** infection is unknown. Our data show that **RSV** colocalizes with intercellular adhesion molecule-1 (**ICAM**-1) on the HEp-2 epithelial cell surface. Furthermore, a neutralizing anti-**ICAM**-1 mAb significantly inhibits **RSV** infection and infection-induced secretion of proinflammatory chemokine RANTES and mediator ET-1 in HEp-2 cells. Similar decrease in **RSV** infection is also observed in A549, a type-2 alveolar epithelial cell line, and NHBE, the normal human bronchial epithelial cell line when pretreated with anti-**ICAM**-1 mAb prior to **RSV** infection. Incubation of virus with soluble **ICAM**-1 also significantly decreases **RSV** infection of epithelial cells. Binding studies using ELISA indicate that **RSV** binds to **ICAM**-1, which can be inhibited by an **antibody** to the fusion F protein and also the recombinant F protein can bind to soluble **ICAM**-1, suggesting that **RSV** interaction with **ICAM**-1 involves the F protein. It is thus concluded that **ICAM**-1 facilitates **RSV** entry and infection of human epithelial cells by binding to its F protein, which is important to viral replication and infection and may lend itself as a therapeutic target.

AN 2001:104926 BIOSIS

DN PREV200100104926

TI Blocking intercellular adhesion molecule-1 on human epithelial cells decreases respiratory syncytial virus infection.

AU Behera, Aruna K. (1); Matsuse, Hiroto (1); Kumar, Mukesh (1); Kong, Xiaoyuan (1); Lockey, Richard F. (1); Mohapatra, Shyam S. (1)

CS (1) Divisions of Allergy and Immunology, Department of Internal Medicine, College of Medicine, University of South Florida, VA Hospital, Tampa, FL, 33612 USA

SO Biochemical and Biophysical Research Communications, (January 12, 2001) Vol. 280, No. 1, pp. 188-195. print.
ISSN: 0006-291X.

DT Article

LA English

SL English

L5 ANSWER 2 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AB Respiratory syncytial virus (**RSV**) infection is associated with epithelial cell death and vigorous inflammation. In mouse models, and in immunosuppressed patients, CD8+ T cells are necessary for **RSV** clearance. In vitro, **RSV** has been shown to induce expression of several proteins on the respiratory epithelial cell, including **RSV** proteins, **ICAM**-1, and MHC class I, that can potentially interact with CD8+ T cells in initiating apoptosis of the target cell. One mechanism of T-cell-directed cell death is the interaction of FasL on the CD8+ T lymphocytes and Fas expressed on the target cell. In order to determine the ability of **RSV** to induce Fas on the respiratory epithelium, we studied the **RSV** infection of a human respiratory epithelial cell line (A549) in vitro. Fas mRNA and protein levels are increased two-to-fourfold following **RSV** infection, and transcriptional upregulation of Fas was demonstrated using promoter/reporter gene constructs. **RSV** infection directly resulted in cellular apoptosis, and the frequency of apoptotic cells was further increased by cross-linking with **antibodies** to Fas. These data demonstrate that **RSV** infection induces cellular apoptosis and suggest that interactions of surface Fas with T cells may further augment this process in vivo.

AN 1999:252064 BIOSIS

DN PREV199900252064

TI Induction of CD95 (Fas) and apoptosis in respiratory epithelial cell cultures following respiratory syncytial virus infection.

AU O'Donnell, D. R.; Milligan, L.; Stark, J. M. (1)

CS (1) Division of Pulmonary Medicine, Allergy and Clinical Immunology, Children's Hospital Medical Center, 3333 Burnet Avenue OSB5, Cincinnati, OH, 45229-3039 USA
SO Virology, (April 25, 1999) Vol. 257, No. 1, pp. 198-207.
ISSN: 0042-6822.
DT Article
LA English
SL English

L5 ANSWER 3 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB The causative agents of acute respiratory infections (ARI) in infants and children are mostly thought to be viruses. Some ARI in adult patients may be caused by bacteria but most often the causes are virus infections. When ARI affect immunocompromised patients or the elderly the mortality rates are significantly higher than in immunocompetent individuals. Many types of viruses cause ARI. Among them, influenza viruses A and B and respiratory syncytial virus (**RSV**) are thought to be the most important because of the severity of illness after infection and their high communicability in the human population. Recently, several novel antiviral drugs against ARI have been developed and some are proceeding in clinical trials. This review covers current investigations into antiviral compounds targeted at several points in the virus life-cycle. This includes PM-523, which broadly inhibits ortho- and paramyxoviruses, two neuraminidase inhibitors for influenza virus, neutralizing **antibody** to **RSV** and chimeric soluble **ICAM** -1-IgA molecules targeted against rhinoviruses.
AN 1998:219856 BIOSIS
DN PREV199800219856
TI Approaches to antiviral chemotherapy for acute respiratory infections.
AU Shigeta, Shiro (1)
CS (1) Dep. Microbiol., Fukushima Med. Coll., Fukushima 960-1295 Japan
SO Antiviral Chemistry & Chemotherapy, (March, 1998) Vol. 9, No. 2, pp. 93-107.
ISSN: 0956-3202.
DT General Review
LA English

L5 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AB The mechanisms of virus-induced enhancement of intercellular adhesion molecule-1 (**ICAM**-1) expression in epithelial cells are unknown. In the present study, the effect of respiratory syncytial virus (**RSV**) infection on the expression of **ICAM**-1 in human pulmonary type II-like epithelial (A549) cells was evaluated. Conditioned **RSV** media (cRSV) produced from growth of **RSV** in A549 cells induced a significant increase in the expression of **ICAM** -1. Treatment of the cells with noninfectious cRSV prepared by ultraviolet (UV) irradiation (UV-cRSV) or ribavirin treatment resulted in the expression of **ICAM**-1 to a similar extent as infectious cRSV. These results suggested that **RSV** induces the synthesis of a soluble mediator(s) that regulates the expression of **ICAM**-1. Cytokine analysis by immunoassay and polymerase chain reaction showed that **RSV** induces the synthesis of interleukin (IL)-1-alpha and -beta, and tumor necrosis factor alpha (TNF-alpha). Preincubation of UV-cRSV with soluble IL-1 receptor (sIL-1r) almost completely blocked the enhancement of **ICAM**-1 expression. Furthermore, simultaneous incubation of infectious purified **RSV** with sIL-1r resulted in a significant reduction in enhancement of **ICAM**-1 expression. Preincubation with neutralizing **antibodies** to IL-1-alpha and -beta, and TNF-alpha showed that the predominant **ICAM**-1 enhancing soluble mediator in UV-cRSV was IL-1-alpha. These experiments provide direct evidence for an autocrine mechanism of enhanced **ICAM**-1 expression in **RSV**-infected epithelial cells that is mediated primarily by IL-1-alpha. Pulmonary epithelial cells may play an important immunoregulatory role in the microenvironment of the lower respiratory

tract infected with **RSV**.

AN 1995:549020 BIOSIS
DN PREV199698563320
TI Interleukin-1-alpha mediates the enhanced expression of intercellular adhesion molecule-1 in pulmonary epithelial cells infected with respiratory syncytial virus.
AU Patel, Janak A. (1); Kunimoto, Masaru; Sim, Tommy C.; Garofalo, Roberto; Eliott, Todd; Baron, Samuel; Ruuskanen, Olli; Chonmaitree, Tasnee; Ogra, Pearay L.; Schmalstieg, Frank
CS (1) Div. Pediatr. Infect. Dis., Child. Hosp., Univ. Tex. Med. Branch, Galveston, TX 77555-0371 USA
SO American Journal of Respiratory Cell and Molecular Biology, (1995) Vol. 13, No. 5, pp. 602-609.
ISSN: 1044-1549.
DT Article
LA English

L5 ANSWER 5 OF 11 MEDLINE
AB The respiratory syncytial virus (**RSV**) causes potentially fatal lower respiratory tract infection in infants. The molecular mechanism of **RSV** infection is unknown. Our data show that **RSV** colocalizes with intercellular adhesion molecule-1 (**ICAM**-1) on the HEp-2 epithelial cell surface. Furthermore, a neutralizing anti-**ICAM**-1 mAb significantly inhibits **RSV** infection and infection-induced secretion of proinflammatory chemokine RANTES and mediator ET-1 in HEp-2 cells. Similar decrease in **RSV** infection is also observed in A549, a type-2 alveolar epithelial cell line, and NHBE, the normal human bronchial epithelial cell line when pretreated with anti-**ICAM**-1 mAb prior to **RSV** infection. Incubation of virus with soluble **ICAM**-1 also significantly decreases **RSV** infection of epithelial cells. Binding studies using ELISA indicate that **RSV** binds to **ICAM**-1, which can be inhibited by an **antibody** to the fusion F protein and also the recombinant F protein can bind to soluble **ICAM**-1, suggesting that **RSV** interaction with **ICAM**-1 involves the F protein. It is thus concluded that **ICAM**-1 facilitates **RSV** entry and infection of human epithelial cells by binding to its F protein, which is important to viral replication and infection and may lend itself as a therapeutic target. Copyright 2001 Academic Press.
AN 2001155101 MEDLINE
DN 21092586 PubMed ID: 11162498
TI Blocking intercellular adhesion molecule-1 on human epithelial cells decreases respiratory syncytial virus infection.
AU Behera A K; Matsuse H; Kumar M; Kong X; Lockey R F; Mohapatra S S
CS Division of Allergy, University of South Florida, College of Medicine, Tampa, Florida 33612, USA.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Jan 12) 280 (1) 188-95.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010322

L5 ANSWER 6 OF 11 MEDLINE
AB Respiratory syncytial virus (**RSV**) infection is associated with epithelial cell death and vigorous inflammation. In mouse models, and in immunosuppressed patients, CD8(+) T cells are necessary for **RSV** clearance. In vitro, **RSV** has been shown to induce expression of several proteins on the respiratory epithelial cell, including **RSV**

proteins, **ICAM**-1, and MHC class I, that can potentially interact with CD8(+) T cells in initiating apoptosis of the target cell. One mechanism of T-cell-directed cell death is the interaction of FasL on the CD8(+) T lymphocytes and Fas expressed on the target cell. In order to determine the ability of **RSV** to induce Fas on the respiratory epithelium, we studied the **RSV** infection of a human respiratory epithelial cell line (A549) in vitro. Fas mRNA and protein levels are increased two-to-fourfold following **RSV** infection, and transcriptional upregulation of Fas was demonstrated using promoter/reporter gene constructs. **RSV** infection directly resulted in cellular apoptosis, and the frequency of apoptotic cells was further increased by cross-linking with **antibodies** to Fas. These data demonstrate that **RSV** infection induces cellular apoptosis and suggest that interactions of surface Fas with T cells may further augment this process in vivo.

AN 1999225659 MEDLINE
DN 99225659 PubMed ID: 10208933
TI Induction of CD95 (Fas) and apoptosis in respiratory epithelial cell cultures following respiratory syncytial virus infection.
AU O'donnell D R; Milligan L; Stark J M
CS Allergy and Clinical Immunology, Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, Ohio, 45229-3039, USA.
SO VIROLOGY, (1999 Apr 25) 257 (1) 198-207.
Journal code: XEA; 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990519

L5 ANSWER 7 OF 11 MEDLINE
AB The causative agents of acute respiratory infections (ARI) in infants and children are mostly thought to be viruses. Some ARI in adult patients may be caused by bacteria but most often the causes are virus infections. When ARI affect immunocompromised patients or the elderly the mortality rates are significantly higher than in immunocompetent individuals. Many types of viruses cause ARI. Among them, influenza viruses A and B and respiratory syncytial virus (**RSV**) are thought to be the most important because of the severity of illness after infection and their high communicability in the human population. Recently, several novel antiviral drugs against ARI have been developed and some are proceeding in clinical trials. This review covers current investigations into antiviral compounds targeted at several points in the virus life-cycle. This includes PM-523, which broadly inhibits ortho- and paramyxo-viruses, two neuraminidase inhibitors for influenza virus, neutralizing **antibody** to **RSV** and chimeric soluble **ICAM**-1-IgA molecules targeted against rhinoviruses.
AN 1999092540 MEDLINE
DN 99092540 PubMed ID: 9875381
TI Approaches to antiviral chemotherapy for acute respiratory infections.
AU Shigeta S
CS Department of Microbiology, Fukushima Medical College, Japan.
SO ANTIVIRAL CHEMISTRY AND CHEMOTHERAPY, (1998 Mar) 9 (2) 93-107. Ref: 87
Journal code: C79; 9009212. ISSN: 0956-3202.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals

EM 199902
ED Entered STN: 19990216
Last Updated on STN: 19990216
Entered Medline: 19990202

L5 ANSWER 8 OF 11 MEDLINE
AB The mechanisms of virus-induced enhancement of intercellular adhesion molecule-1 (**ICAM**-1) expression in epithelial cells are unknown. In the present study, the effect of respiratory syncytial virus (**RSV**) infection on the expression of **ICAM**-1 in human pulmonary type II-like epithelial (A549) cells was evaluated. Conditioned **RSV** media (cRSV) produced from growth of **RSV** in A549 cells induced a significant increase in the expression of **ICAM** -1. Treatment of the cells with noninfectious cRSV prepared by ultraviolet (UV) irradiation (UV-cRSV) or ribavirin treatment resulted in the expression of **ICAM**-1 to a similar extent as infectious cRSV. These results suggested that **RSV** induces the synthesis of a soluble mediator(s) that regulates the expression of **ICAM**-1. Cytokine analysis by immunoassay and polymerase chain reaction showed that **RSV** induces the synthesis of interleukin (IL)-1 alpha and -beta, and tumor necrosis factor alpha (TNF-alpha). Preincubation of UV-cRSV with soluble IL-1 receptor (sIL-1r) almost completely blocked the enhancement of **ICAM**-1 expression. Furthermore, simultaneous incubation of infectious purified **RSV** with sIL-1r resulted in a significant reduction in enhancement of **ICAM**-1 expression. Preincubation with neutralizing **antibodies** to IL-1 alpha and -beta, and TNF-alpha showed that the predominant **ICAM**-1 enhancing soluble mediator in UV-cRSV was IL-1 alpha. These experiments provide direct evidence for an autocrine mechanism of enhanced **ICAM**-1 expression in **RSV**-infected epithelial cells that is mediated primarily by IL-1 alpha. Pulmonary epithelial cells may play an important immunoregulatory role in the microenvironment of the lower respiratory tract infected with **RSV**.
AN 96054927 MEDLINE
DN 96054927 PubMed ID: 7576697
TI Interleukin-1 alpha mediates the enhanced expression of intercellular adhesion molecule-1 in pulmonary epithelial cells infected with respiratory syncytial virus.
AU Patel J A; Kunimoto M; Sim T C; Garofalo R; Eliott T; Baron S; Ruuskanen O; Chonmaitree T; Ogra P L; Schmalstieg F
CS Department of Pediatrics, University of Texas Medical Branch, Galveston 77555-0371, USA.
NC AI-15939 (NIAID)
DC-02129 (NIDCD)
HD-27841 (NICHD)
SO AMERICAN JOURNAL OF RESPIRATORY CELL AND MOLECULAR BIOLOGY, (1995 Nov) 13 (5) 602-9.
Journal code: AOB; 8917225. ISSN: 1044-1549.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199512
ED Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951206

L5 ANSWER 9 OF 11 USPATFULL
AB Nitric oxide generating compounds or compounds which induce in situ synthesis of nitric oxide can be used to inhibit rhinovirus infection. Nitric oxide has the ability to inhibit both viral replication as well as the synthesis of cytokines, in particular the proinflammatory cytokines. Thus the symptoms of rhinovirus infections can be ameliorated by treatments to increase nitric oxide in the respiratory tract.

AN 2001:136694 USPATFULL
TI Nitric oxide inhibits rhinovirus infection
IN Sanders, Scherer P., Lutherville, MD, United States
Proud, David, Baltimore, MD, United States
PA The Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)
PI US 6277891 B1 20010821
AI US 1998-113310 19980710 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Travers, Russell
LREP Banner & Witcoff
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 38 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 1117
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 10 OF 11 USPATFULL
AB The invention provides compositions of a non-adenoviral vector containing a polynucleotide sequence encoding adenoviral pTP operationally linked domain. The invention also provides compositions of an adenoviral pTP binding domain. The invention also provides methods for increasing the expression of a polynucleotide by expressing the polynucleotide in a non-adenoviral vector containing an adenoviral pTP binding domain in the presence of adenoviral pTP. The invention additionally provides methods to increase expression of a heterologous polynucleotide in an individual by obtaining cells from the individual, genetically altering the cells to express a non-adenoviral vector containing an adenoviral pTP binding domain and a gene encoding pTP and readministering the genetically altered cells to the individual.
AN 2000:138079 USPATFULL
TI Methods and compositions for enhanced stability of non-adenoviral DNA
IN Kay, Mark A., Seattle, WA, United States
Lieber, Andre, Seattle, WA, United States
PA University of Washington, Seattle, WA, United States (U.S. corporation)
PI US 6132989 20001017
AI US 1997-972657 19971118 (8)
RLI Continuation-in-part of Ser. No. US 1997-867012, filed on 2 Jun 1997, now abandoned
PRAI US 1996-18928P 19960603 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Yucel, Remy
LREP Campbell & Flores LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 1601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 11 OF 11 USPATFULL
AB Humanized anti-CD11a antibodies and various uses therefor are disclosed. The humanized anti-CD11a antibody may bind specifically to human CD11a I-domain, have an IC50(nM) value of no more than about 1 nM for preventing adhesion of Jurkat cells to normal human epidermal keratinocytes expressing ICAM-1, and/or an IC50 (nM) value of no more than about 1 nM in the mixed lymphocyte response assay.
AN 2000:31527 USPATFULL
TI Humanized anti-CD11a antibodies
IN Jardieu, Paula M., San Francisco, CA, United States
Presta, Leonard G., San Francisco, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)

PI US 6037454 20000314
AI US 1997-974899 19971120 (8)
PRAI US 1996-31971P 19961127 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Saunders, David; Assistant Examiner: VanderVegt, F. Pierre
LREP Lee, Wendy M., Schwartz, Timothy R.
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 3180
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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